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Review Article

Gorlin Goltz Syndrome A Rare Entity: Case Report and Review of Literature

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Abstract

Gorlin-Goltz syndrome (GGS) is a rare uncommon multisystemic disease with an autosomal dominant inherited disorder characterized by the presence of multiple odontogenic keratocysts, basal cell nevi carcinomas and skeletal abnormalities are unique features of this autosomal dominant inherited disorder known as Goltz syndrome. Genetically abnormalities were noticed in the long arm of chromosome 9 and failure in mutation of human gene PTCH1 gene. Presence of major and minor criteria (Table 2) playing a major role in diagnosis of this kind of syndrome. Presenting a case of 18-year-old boy in favor of Gorlin syndrome having one major and six minor criteria adding to confirm diagnosis. Along with clinical features, radiological findings with the help of orthopantomogram, CT scan, chest X-ray help in the diagnosis of this particular syndrome, thus helps in prevention of recurrence and better survival rates because of early detection.

Keywords: Gorlin-Goltz Syndrome; Odontogenic Keratocysts; Basal Cell Nevi Carcinomas; Polysyndactaly; Bifid Ribs; Hypertelorism; Frontal Bossing

Abbreviations

GGS: Gorlin - Goltz Syndrome; OKCs: Odontogenic Keratocysts; PTCH Gene: Patched Gene; BCCs: Basal Cell Carcinomas; CBCT: Cone Beam Computed Tomography; Hh: Hedgehog; Smo: Smoothened

Introduction

Multiple cystic lesions present on radiographs lead us to think about this kind of syndrome without any prominent clinical findings. Presence of multiple cysts in other syndromes like Ehler-Danlos syndrome, Noonan syndrome, orofacial digital syndrome, Simpson-Golabi-Behmel syndrome or other syndromes but different clinical features made this syndrome unique. GGS involves other systems in body characterized by a predisposition to neoplasms and other developmental abnormalities. It is differentiated from other syndromes on the basis of major and minor criterions for diagnosis and its hereditary correlation [1,2].

Studies show the presence of multiple cystic lesions without any syndromic characteristics, 8.1% were associated with NBCCS,

and from them 7.6% had recurrence [3]. According to Gorlin and Goltz, this lesion had several features like multiple nevoid basal cell carcinomas (BCCs), bifid ribs, jaw cysts, etc.; that is why this lesion is termed Gorlin–Goltz syndrome. As it is inherited as autosomal dominant lesion, it is characterized by total penetrance and variable expressivity. Being a dental surgeon, we could accidentally find the presence of multiple odontogenic keratocysts (OKCs), which is the only manifestation of the syndrome [4,5]. That is why its knowledge is necessary to contribute towards right diagnosis and prevention of further complications.

Different authors suggest various treatment options to deal with the presence of OKCs. Depending on the size of the cystic lesion decision regarding enucleation or marsupialization is made. For smaller lesions enucleation is better treatment option while for larger ones marsupialization is preferred. In cases of enucleation, chemical cauterization with the help of Carnoy's solution is preferred to prevent recurrence. To deal with syndromic OKCs, a team of dental, medical, and genetics specialties is required. A regular followup is advised since these lesions have a high recurrence rate [6,7].

We are presenting a case of Gorlin–Goltz syndrome and will talk about its etiopathogenesis, diagnostic criterias and the difference in the treatment for syndromic and asyndromic OKCs.

Case Report

An 18-year-old male patient came to our private clinic with chief complaint of swelling on right side of face since 4-5 months. The swelling which was initially smaller in size, presently shows a larger dimension with progression of time. The history of present illness revealed that there was swelling in the upper right back teeth region since 4 months for which he came to our clinic. The patient has no history of hot water fomentation. The patient does not have any significant medical history. He did not have significant family history. Complete clinical examination was carried out. Extraorally frontal bossing, hypertelorism, depressed nasal bridge, polysyndactaly in left leg little finger were found [Figure 1 and Figure 2]. There were diffuse swellings seen on right side maxillary region measuring about 1 cm × 1 cm in size. There was no presence of perforation and discharge. On palpation it was hard and nontender. On intraoral examination diffused swellings were evident in the upper right back teeth region extending from 16 to 18 teeth region. Mucosa over the swellings was normal with presence of serous discharge. On palpation, all the inspection findings were confirmed and the swelling was fluctuant and nontender with diffuse borders. Spacing was present in maxillary incisor region along with peg lateral incisor irt 22 and missing teeth was 12 whereas 18, 28, 38 and 48 were impacted [Figure 3].

Figure 1: Front profile.

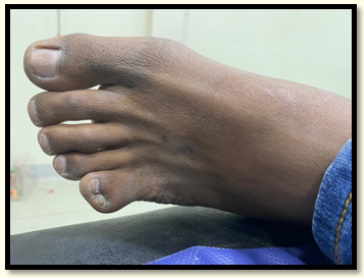

Figure 2: Polysyndactaly of little finger in left leg.

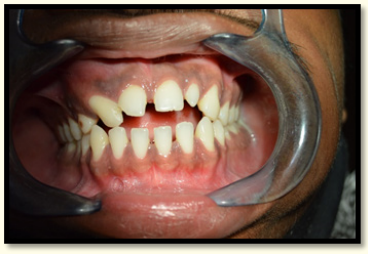

Figure 3: Intraoral picture.

Along with clinical examinations, radiographic examination with the advent of panoramic radiograph, Cone beam computed tomography (CBCT) scan and chest x-ray was done. On evaluation of radiographs, it was observed that there were multiple unilocular radiolucencies of various sizes located at the lower right body angle region (adjacent to 48), left body angle region (adjacent to 38), and upper right, left and front teeth region (adjacent to 17,11 and 21, 27) [Figure 4]. Chest x-ray was normal and has no significant findings. Based on provisional diagnosis of multiple odontogenic cysts, enucleation of the cyst followed by chemical cauterization using carnoy's solution was planned. Gross examination revealed multiple bits of whitish brown soft tissue specimens and cystic lining, together measuring about 2 cm × 2 cm x 0.1 cm in size, which are whitish to creamish in color and thicker in consistency. Microscopic examination showed a cystic lining that is thin and has stratified squamous cell lining with pinkish areas of keratinous material. Cystic wall has focal hyperplasia of lining cells and keratinous material with foci of chronic inflammatory cells mainly lymphocytes were seen [Figure 5].

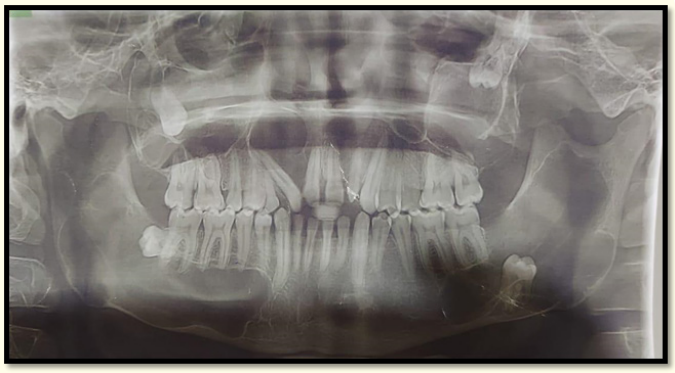

Figure 4: Orthopantomogram (OPG).

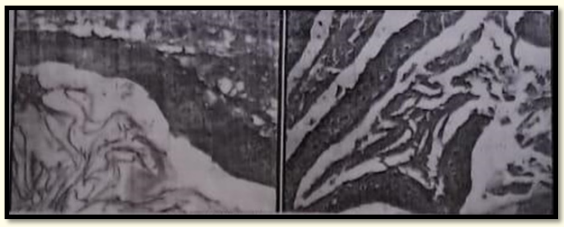

Figure 5: Histopathological examination.

Histopathologically, a diagnosis of multiple odontogenic keratocysts was confirmed in all clinically present cysts. A correspondence was seen among clinical, radiographical and histopathological findings, hence the diagnosis was in favor of Gorlin-Goltz syndrome.

Discussion

Studies have shown that incidence of Gorlin Goltz syndrome is about 1 in 50,000–150,000 with multiple OKCs as one of the early manifestations, making it easy for the dentists in early detection followed by management of this syndrome [1,8].

This lesion has a high penetrance and variable expressivity. The patched tumor suppressor gene (PTCH), which is a human homologue of the Drosophila gene mapped to chromosome 9q21-23, mutations in which results in the cause of this lesion. Its inheritance is autosomal dominant.

Gorlin–Goltz syndrome shows six clinical manifestations of different spectrum that can be seen in various patients as shown in table [Table 1]. These clinical manifestations are divided into major and minor diagnostic criterias. Evans., *et al*. and Kimonis., *et al*. suggested that to diagnose a patient with Gorlin–Goltz syndrome, two major or one major and two minor criteria should be present in patient [Table 2]. In case of our patient, the diagnosis was confirmed as he matched one major criteria (multiple OKCs) and six minor criteria (frontal bossing, depressed nasal bridge, ocular hypertelorism, prominance in supra orbital ridge, polysyndactaly, mild mandibular prognathism) [911].

Literature review of clinical manifestations showed that Gorlin–Goltz syndrome is usually seen in younger age group ranging from 10 - 30 years. Our patient was 18 years old. Generally, females are predominantly affected, whereas ours was a male patient. The commonest site of OKCs for Gorlin–Goltz syndrome is maxillary molar region; our case presented with multiple cysts bilaterally at posterior mandible and ramus area, bilaterally at maxillary molar area and maxillary anterior region too [12,13].

Radiologic findings of OKCs show unilocular, welldefined radiolucent lesions, usually associated with unerupted tooth. Our case showed unilocular radiolucency in relation to an unerupted right

Anomalies	Manifestations
Cutaneous	Basal cell nevi, basal cell carcinomas, benign dermal cysts and tumors, dermal calcinosis, and palmar and plantar keratosis
Dental	Multiple OKCs, mild mandibular prognathism
Osseous	Frontal bossing, bifid ribs, spina bifida, kyphoscoliosis, and brachymetacarpalism
Eye	Hypertelorism, congenital blindness, and internal strabismus
Neural	Dural calcification, mental retardation, and medulloblastoma
Sexual	Hypogonadism, ovarian tumors

Table 1: Clinical manifestations of Gorlin–Goltz syndrome.

Major Criteria	Minor Criteria
Multiple basal cell carcinomas or one BCC below 20 years	Macrocephaly (adjusted for height)
Multiple OKCs	Congenital malformation: Cleft lip or palate, frontal bossing, and moderate or severe hypertelorism
Three or more palmar or plantar pits	Other skeletal abnormalities: Sprengel's deformity, marked pectus deformity, marked syndactyly of the digits
Bilamellar calcification of the falx cerebri	Radiological abnormalities: Bridging of the sella turcica, vertebral anomalies such as hemivertebrae, fusion or elongation of the vertebral bodies, modeling defects of the hands, and feet or flame shaped hands or feet
Bifid, splayed, or fused ribs	Medulloblastoma
Close relative having syndromic OKCs characteristics	Ovarian fibroma

Table 2: Major and minor diagnostic criterion of Gorlin–Goltz syndrome.

and left third molars in angle ramus region, in maxillary right and left third molar region along with upper anterior teeth region. Generally, "multiple cysts" means more than one cyst is present at a time, whereas in this case multiple cysts means presence of more than one cyst in one's lifespan [4,13,14].

Histologically, OKCs show corrugated para or orthokeratinized surface, almost uniform thickness of the epithelium, basal cells shows tomb stone or picket fence arrangement. Few cases show the presence of daughter or satellite cell lining in the underlying connective tissue and these cysts has more recurrence rate. Parakeratotic type of OKCs are more common and more aggressive than orthokeratotic type of OKCs. In case of Gorlin–Goltz syndrome, parakeratotic OKCs are seen. The major differences between OKCs associated with Gorlin–Goltz syndrome and solitary isolated OKCs are listed in the following table 3 [14,15]. Our case showed a cystic lining that is thin and has stratified squamous cell lining with pinkish areas of keratinous material. Cystic wall has focal hyperplasia of lining cells and keratinous material with foci of chronic inflammatory cells mainly lymphocytes were seen.

Feature	Syndromic OKCs	Solitary OKCs
Age	Younger individuals	Middle or older aged individuals
Cysts	Multiple in number	Single
Site	Maxillary posterior region commonly	Mandibular posterior region
Recurrence rate	Higher (82%)	Lower (61%)
Epithelium	Less thickness	More thickness
Odontogenic islands	More frequent	Less

Table 3: Differences between syndromic OKCs and solitary OKCs.

Various conservative approaches have been utilised for young patients with large cysts to prevent loss of soft and hard tissues including the teeth. These include marsupialization, decompression, enucleation with neoadjuvant therapy using Carnoy's solution, cryotherapy or electrocautery, peripheral ostectomy with or without Carnoy's solution, jaw resection and surgical excision of the keratocyst. We treated cysts by enucleation with adjuvant application of Carnoy's solution. The studies have shown that multiple OKCs are detected almost 10 years prior to the appearance of other symptoms of Gorlin–Goltz syndrome so it is considered as a important and utmost diagnostic criteria. Hence, a surgeon has a pivot role in treating this type of syndromic cases as he will be the first person to detect such oral findings and predict occurrence of syndrome in future. Comprehensive treatment of this syndrome requires a teamwork with dental and medical opinion as well as genetic counseling [14,16].

Conclusion

Gorlin-Goltz syndrome is an autosomal dominant variant heredity disorder with multiple major and minor diagnostic criteria. Thorough extraoral and intraoral examinations along with various radiographic examination help in proper diagnosis of the condition. We suggest that patients with multiple OKCs should be evaluated thoroughly as they are the major diagnostic criteria of Gorlin–Goltz syndrome and early findings in this syndrome. So proper diagnosis and early treatment is must in this patients to prevent recurrence and avoid various complications.

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Conflicts of Interests

The authors declare no conflict of interest.

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